

## What is claimed is:

~~1.~~ A method for enhancing cytotoxicity elicited by a therapeutic antibody *in vivo* in a subject, which method comprises disrupting activation of SHIP by Fc-gamma-receptor IIB (FcγRIIB).

5                   2. The method according to claim 1, wherein the SHIP activation by FcγRIIB results from antibody binding to FcγRIIB.

3. The method according to claim 2, wherein antibody binding is inhibited by a competitive inhibitor.

~~4.~~ The method according to claim 2, wherein antibody binding is inhibited by modifying the Fc portion of the antibody to reduce its affinity for FcγRIIB.

5. The method according to claim 1, wherein SHIP activation by FcγRIIB is disrupted by inhibiting the expression of FcγRIIB.

6. The method according to claim 5, wherein FcγRIIB expression is disrupted with an antisense nucleic acid specific for the γIIB chain mRNA.

15                   7. The method according to claim 5, wherein FcγRIIB expression is disrupted with an intracellular antibody specific for the γIIB chain.

8. The method according to claim 1, wherein SHIP activation is inhibited by an inositol phosphatase inhibitor.

20                   9. The method according to claim 1, wherein SHIP activation is inhibited by inhibiting SHIP expression.

10. The method according to claim 1, wherein the antibody is an anti-tumor antibody.

11. The method according to claim 10, wherein the antibody is specific for a tumor cell growth receptor.

5 12. The method according to claim 11, wherein the antibody is specific for a HER2/neu growth factor receptor.

13. The method according to claim 11, wherein the antibody is specific for a CD20 B cell antigen.

10 14. The method according to claim 1, wherein the antibody binds to human activating Fc receptors.

15 15. The method according to claim 14, wherein the subject expresses human Fc receptors.

16 16. An antibody with a variant Fc region, which antibody binds FcγRIIB with reduced affinity.

17 17. The antibody of claim 16, which binds activating Fc-receptors with at least the same affinity as wildtype antibody.

18. The antibody of claim 16, which is an anti-tumor antibody.

19. The antibody of claim 18, which is specific for a tumor cell growth receptor.

20. The antibody of claim 19, which is specific for a HER2/neu growth factor receptor.

21. The antibody of claim 19, which is specific for a CD20 B cell antigen.

11/11/2003 11:11:11 AM